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GROUP 1700

Application Serial No.: 10/039,984
Applicant : Olga G. Petrovskaja and Anil Kumar
Filed : October 29, 2001
Group Art Unit : 1712
Examiner : Philip C. Tucker
Atty. Docket No. : 1651A1
Title : NOVEL INDENO-FUSED PHOTOCHROMIC
NAPHTHOPYRANS

DECLARATION UNDER 37 CFR 1.131

Olga G. Petrovskaja and Anil Kumar declare as follows:

That we are the co-inventors of the subject matter disclosed and claimed in captioned Application Serial No. 10/039,984, filed October 29, 2001 which claims priority to provisional Application Serial No. 60/258,973 filed December 29, 2000;

We completed the invention prior to November 28, 2000, which is the publication date of JP 2000-327675 cited against the captioned application;

As evidence of the reduction to practice, attached are various notebook pages with the dates blocked out, all prior to November 28, 2000;

Experiment 817-132a at the bottom of page 156

Preparation of 3,3,9-triphenyl-3H-9H-indeno-

[3',2':3,4]naphtho[1,2-b]pyran

The following materials were added to a reaction flask in the order and manner described as follows:

<u>Materials</u>	<u>Amount</u>
chloroform	40 mL
7-phenyl-benzo(a)fluoren-2-ol ⁽¹⁾	0.4 gram
p-dodecylbenzene sulfonic acid	catalytic amount
1,1-diphenyl-2-propyn-1-ol	0.21 gram

- (FN1) 7-Phenyl-benzo(a)fluoren-2-ol was prepared in Experiment 817-132 on the top of page 156 which describes the addition of the product of Experiment 817-126, i.e., 7-phenyl-1,11b-dihydrobenzyl(a)fluoren-2-one⁽²⁾, to a reaction flask containing tetrahydrofuran (20 mL), ethanol (10 mL) and potassium hydroxide (0.35 gram) and was stirred overnight, the resulting reaction mixture was acidified and the recovered product (about 0.4 gram) was a red oil;
- (FN2) 7-Phenyl-1,11b-dihydrobenzyl(a)fluoren-2-one was prepared in Experiment 817-126 on page 150 which describes the addition of the product of Experiment 817-124, i.e., diphenyl-(1-(4-methoxy)naphthyl)methanol⁽³⁾ to a reaction flask containing phosphoric acid and heating the contents to 70°C for 2 hours, at which time it was determined that no reaction occurred, the contents of the reaction flask were heated to about 110°C for 2 hours and it was determined that the starting material was gone, the reaction mixture was poured into water, the resulting organic precipitate was separated by filtration and chromatographed on a silica column first with hexane and a second time with 10% ethylacetate in hexane as the eluant, a blue fraction was collected and upon removal of solvents a white solid formed, Nuclear Magnetic Resonance (NMR) analysis showed the product to have a structure consistent with 7-phenyl-1,11b-dihydrobenzyl(a)fluoren-2-one;
- (FN3) Diphenyl-(1-(4-methoxy)naphthyl)methanol was prepared in Experiment 817-124 on page 148 which describes the addition of the product of Experiment 817-123, i.e., phenyl-1-(4-methoxynaphthyl) methanone⁽⁴⁾, (10.3 millimoles) to a reaction flask containing 60 milliliters (mL) of anhydrous tetrahydrofuran and cooling the contents of the reaction flask to -5°C, phenyllithium (5.7 milliliters of a 1.8 molar solution in cyclohexane-ether) was added to the reaction flask, further cooling was stopped, the reaction mixture was stirred overnight and allowed to warm to room temperature; analysis of the resulting product revealed that it was necessary to add more phenyllithium (in excess) to produce diphenyl-(1-(4-methoxy)naphthyl)methanol which was identified by Mass Spectroscopy;
- (FN4) Phenyl-1-(4-methoxynaphthyl) methanone was prepared in Experiment 817-123 on page 147 which describes the addition of 1-methoxynaphthalene (20.7 millimoles), benzoyl chloride (34.4 millimoles) and graphite (10 grams) to a reaction flask and heating the reaction mixture at 125°C for 20 hours; the resulting reaction mixture was filtered, the recovered graphite was washed with ethyl acetate, the organic layer of the reaction mixture was separated, washed with aqueous sodium bicarbonate and dried, organic solvents were removed, the resulting material was washed with hexanes to remove chlorobenzene, and the resulting reaction mixture was separated by column chromatography using 10% ethylacetate in hexane as the eluant to produce 3.5 grams of phenyl-1-(4-

methoxynaphthyl) methanone containing a residual amount of chlorobenzene as identified by Mass Spectroscopy;

After the addition of the materials, the resulting reaction mixture was stirred for 24 hours, separated by column chromatography using dichloroethylene/hexane/ethylacetate as the eluant in the following proportions 4/5/1, the top fraction was collected and further purified by column chromatography using dichloroethylene/hexane as the eluant in a ratio of 1:2, the top fraction was again collected and processed to yield 0.21 gram of product that was subsequently identified as 3,3,9-triphenyl-3H-9H-indeno[3',2':3,4]naphtho[1,2-b]pyran;

Experiment 817-134 at the top of page 158

Preparation of 3,3-di(4-methoxyphenyl)-9-phenyl-3H-9H-indeno[3',2':3,4]naphtho[1,2-b]pyran

The following materials were added to a reaction flask in the order and manner described as follows:

<u>Materials</u>	<u>Amount</u>
chloroform	40 mL
7-phenyl-benzo(a)fluoren-2-ol (prepared in FN1)	0.31 gram
p-dodecylbenzene sulfonic acid	catalytic amount
1,1-bis(4-methoxyphenyl)-2-propyn-1-ol	0.27 gram

After the addition of the materials, the resulting reaction mixture was stirred for 24 hours at room temperature, separated by column chromatography using dichloroethylene/hexane as the eluant in a ratio of 1:2, the top fraction was collected and processed to yield 0.25 gram of product that was subsequently identified as 3,3-di(4-methoxyphenyl)-9-phenyl-3H-9H-indeno[3',2':3,4]naphtho[1,2-b]pyran;

Experiment 817-136 on page 161

Preparation of 3-(4-methoxyphenyl)-3,9-diphenyl-3H-9H-indeno[3',2':3,4]naphtho[1,2-b]pyran

The following materials were added to a reaction flask in the order and manner described as follows:

CHARGE 1

<u>Materials</u>	<u>Amount</u>
chloroform	200 mL
7-phenyl-benzo(a)fluoren-2-ol (prepared in FN1)	0.15 gram
p-dodecylbenzene sulfonic acid	50 milligram
1-phenyl,1-(4-methoxyphenyl)-2-propyn-1-ol	0.24 gram

CHARGE 2

<u>Materials</u>	<u>Amount</u>
1-phenyl,1-(4-methoxyphenyl)-2-propyn-1-ol	0.24 gram

After the addition of CHARGE 1, the resulting reaction mixture was stirred for 24 hours at room temperature, CHARGE 2 was added and the reaction mixture was stirred for 6 days at room temperature, the resulting reaction mixture was separated by column chromatography using dichloroethylene/hexane as the eluant in a ratio of 1:2 and the fraction collected was processed to yield 0.1 gram of material, NMR analysis showed the product to have a structure consistent with 3-(4-methoxyphenyl)-3,9-diphenyl-3H-9H-indeno[3',2':3,4]naphtho[1,2-b]pyran;

Experiment 817-143 on page 168

Preparation of 3-(4-morpholinophenyl)-3,9-diphenyl-3H-9H-indeno[3',2':3,4]naphtho[1,2-b]pyran

The following materials were added to a reaction flask in the order and manner described as follows:

CHARGE 1

<u>Materials</u>	<u>Amount</u>
chloroform	80 mL
7-phenyl-benzo(a)fluoren-2-ol (prepared in FN1)	1.23 gram
p-dodecylbenzene sulfonic acid	60 milligram

CHARGE 2

<u>Materials</u>	<u>Amount</u>
chloroform	150 mL
1-phenyl,1-(4-morpholinophenyl)-2-propyn-1-ol	1.17 gram

CHARGE 3

<u>Materials</u>	<u>Amount</u>
p-dodecylbenzene sulfonic acid	110 milligram

After the addition of CHARGE 1, CHARGE 2 was added in a dropwise fashion with stirring over a 2 hour period, the resulting reaction mixture was stirred overnight, CHARGE 3 was added and the resulting reaction mixture was stirred overnight, stirring was continued for 2 additional days, solvents were removed and the product was separated by column chromatography using 10% ethylacetate in hexanes as the eluant, the recovered material was triturated in methyl cyanide twice to yield 0.61 gram of material, Proton and Carbon-13 NMR and MS analysis showed the product to have a structure consistent with 3-(4-morpholinophenyl)-3,9-diphenyl-3H-9H-indeno[3',2':3,4]naphtho[1,2-b]pyran;

Experiment 817-158 on page 184

Preparation of 3,3-di(4-methoxyphenyl)-9-(3-methoxyphenyl)-11-methoxy-3H-9H-indeno[3',2':3,4]naphtho [1,2-b]pyran;

The following materials were added to a reaction flask in the order and manner described as follows:

CHARGE 1

<u>Materials</u>	<u>Amount</u>
9-methoxy-7-[3-methoxyphenyl]-1,11b-dihydro-benzo(a)fluoren-2-one ⁽⁵⁾	0.37 gram
tetraethoxytitanate in 20 mL of anhydrous toluene	0.57 gram

CHARGE 2

<u>Materials</u>	<u>Amount</u>
Toluene (anhydrous)	10 mL
3,3-di(4-methoxyphenyl)acrylaldehyde	0.5 gram

(FN5) 9-methoxy-7-[3-methoxyphenyl]-1,11b-dihydro-benzo(a)fluoren-2-one was prepared following the procedure used to prepare 7-phenyl-benzo(a)fluoren-2-ol ⁽¹⁾ except that in Experiment 817-123 described in (FN4), 3-methoxybenzoyl chloride was used in place of benzoyl chloride and in Experiment 817-124 described in (FN3), 3-methoxyphenyl magnesium bromide was used in place of phenyl lithium and the procedures of Experiments 817-126 and 817-132 described in (FN2) and (FN1), respectively, were followed;

After the addition of CHARGE 1, the resulting reaction mixture was stirred for 2 days at room temperature and analyzed but none of the desired product was found, the reaction mixture was heated to reflux temperature in toluene for about 6 hours, CHARGE 2 was added and after 2 hours, analysis by thin layer chromatography using dichloroethylene/hexane/ethylacetate as the eluant in the following proportions 4/5/1 showed formation of the photochromic material, product was separated by column chromatography using the aforementioned eluant first followed by the eluant in a proportion of 1/4/15 to yield 0.2 gram of material, MS analysis showed the product to have a structure consistent with 3,3-di(4-methoxyphenyl)-9-(3-methoxyphenyl)-11-methoxy-3H-9H-indeno[3',2':3,4]naphtho [1,2-b]pyran; and

Experiment 817-160 on the bottom of page 185
Preparation of 3-(4-methoxyphenyl)-3-phenyl-9-(3-methoxyphenyl)-
11-methoxy-3H-9H-indeno[3',2':3,4]naphtho [1,2-b]pyran;

The following materials were added to a reaction flask in the order and manner described as follows:

CHARGE 1

<u>Materials</u>	<u>Amount</u>
toluene	100 mL
9-methoxy-7-[3-methoxyphenyl]- benzo(a)fluoren-2-ol (6)	0.74 gram
p-dodecylbenzene sulfonic acid	100 milligrams
1-phenyl,1-(4-methoxyphenyl)-2-propyn-1-ol	0.48 gram

CHARGE 2

<u>Materials</u>	<u>Amount</u>
1-phenyl,1-(4-methoxyphenyl)-2-propyn-1-ol	0.24 gram

(FN6) 9-methoxy-7-[3-methoxyphenyl]-benzo(a)fluoren-2-ol was prepared in Experiment 817-159 at the top of page 185 by the addition of 9-methoxy-7-[3-methoxyphenyl]-1,11b-dihydro-benzo(a)fluoren-2-one (about 1.5 gram) to a reaction flask containing potassium hydroxide (1 gram) and ethanol and diethylether in a 2:1 ratio; after the reaction was complete, solvents were removed and hydrochloric acid (2N) was added to adjust the pH to about 5; ethylacetate extraction yielded about 1 gram of the desired product;

After the addition of CHARGE 1, the resulting reaction mixture was stirred overnight at room temperature, CHARGE 2 was added and the reaction mixture was stirred overnight at room temperature, the product was separated by column chromatography using the ethylacetate/chloroform/hexane in a 1/4/5 ratio and again put through column chromatography using 40% diethylether in hexanes as the eluant, photochromic fractions were recrystallized

from methanol but had to be again put through column chromatography with a large amount of material separating into fractions of 55-85 % purity; Mass Spectroscopy confirmed the structure;

Notebook pages referenced herein are attached in numerical order;

That all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; that all activities related to these statements did occur in the United States; that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Further Declarants say not.

O. Petrovskaya
Olga G. Petrovskaya

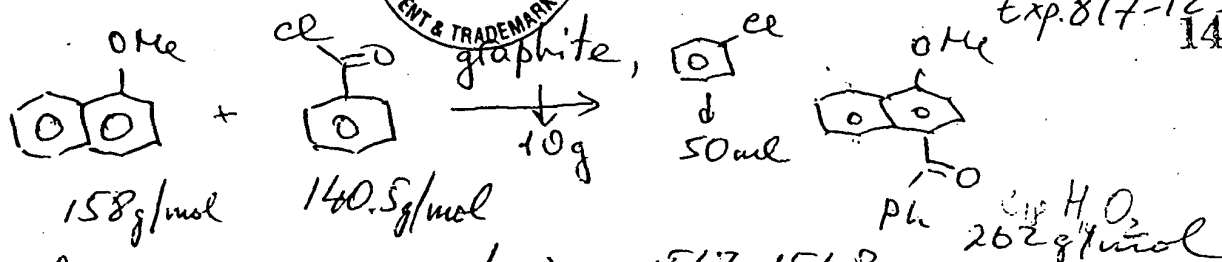
Aug. 1, 03
Date

Anil Kumar
Anil Kumar

8/6/03
Date



Exp. 817-123
147



Chem. Commun. 1997(16), pp 1567-1568

3ml, $\rho=1.09g/ml$ 4ml, $\rho=1.21g/ml$
20.7g 34.4mmol
10.3mmol

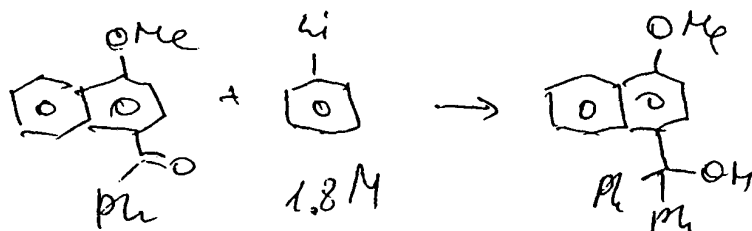
The st. materials were ^{heated} refluxed at 125°C for 20 hrs, then the rxn. mix. was filtered off, ^{graphite} was washed with EtOAc, the solvents removed the org. phase was washed with aq. NaHCO₃ and dried; then org. solvents were stripped off on a rotavap.

TLC in hexane: some Clc1ccccc1 & COc1ccc2ccccc2c1 still present, the major component is a ketone (stains with DNPH (Dinitrophenylhydrazine)). Hexane wash: most Clc1ccccc1 is removed. The rest was put on a column ^{col. EtOAc/hex} Product contains residual amts. of COc1ccc2ccccc2c1? $\Sigma=3.5g$?

$M^+=262$, correct.

O.P.

Handwritten signature: W. Trussard 147-158



262 g/mol
from 10.3 mmol.

5.7 ml = 1 eq.

$C_{24}H_{20}O_2 = 340$ g/mol
288

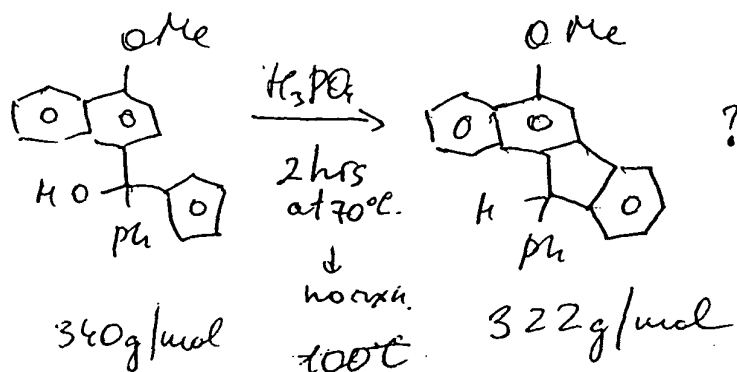
Excess of Ph-Li was added to the st. m. in 60 ml THF at $-5-0^{\circ}\text{C}$. left to warm up to RT & stir overnight.

Problem: crappy PhLi. Rxn. mix. was worked up, more PhLi was added (excess).

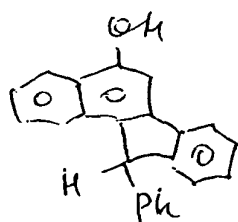
MS: 340. The crude product was taken to the next step.

O. Petrovskaya

me sl

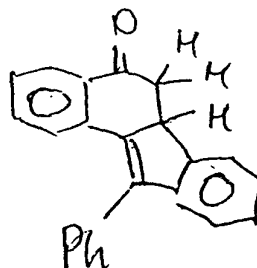


2 hrs at $\sim 110^\circ\text{C}$. \rightarrow st.m. gone, a
 fluorescent (under long-wave UV)
 spot appeared. ^{Exy mix is poured into H_2O , then extracted.} Column 1) hexane
 2) 10% Et_2O in hexane. A blue fraction
 is collected. Upon rotavaporing it
 forms a white solid. MS: 308,



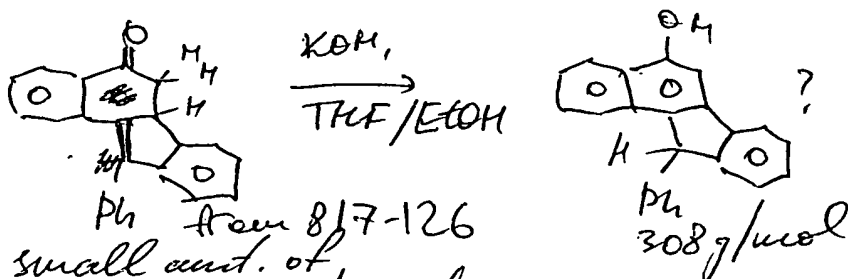
???

By NMR:

How to
isomerize it?

O. Petruskas

Ma 21



small amt. of
st. m. was stirred

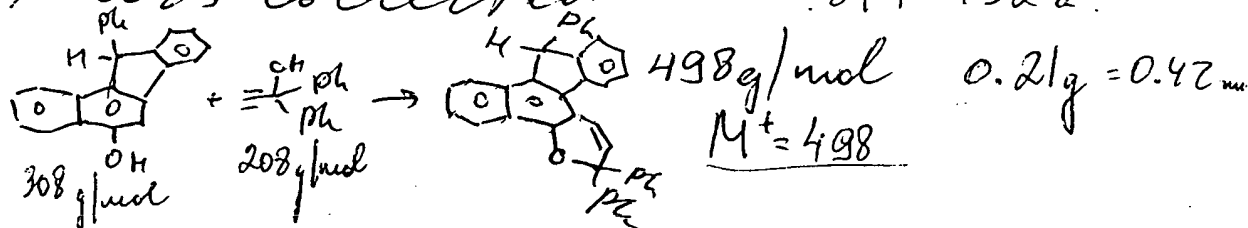
with 20 ml THF / 10 ml EtOH and 0.35 g KOH overnight.

the rxn. mix was acidified. Spot to spot
conversion. No st. m. present. The pro-

duct reacts with 72-PA to yield a PC.
(by TLC, in hex/EtOAc, $R_{f, PC} = 5/1/4$)

The product (0.4 g of red oil (with some residual
EtOAc; ~ 1 mmol) was dissolved in 40 ml CH_2Cl_2 ,
cat. DBSA (dodecylbenzene sulfonic acid) was added
and 1 mmol of $\equiv \frac{CH}{Ph}$ (208 g/mol) was added.
Part of the rxn. mixture was lost (spilled
while stirring). The rxn. mix. was put
on a column after 1 day, CH_2Cl_2 :hex:
EtOAc (4:5:1); the top fraction was
collected. It was further purified
on a column (CH_2Cl_2 /hex. = 1:2), the top
fr. was collected.

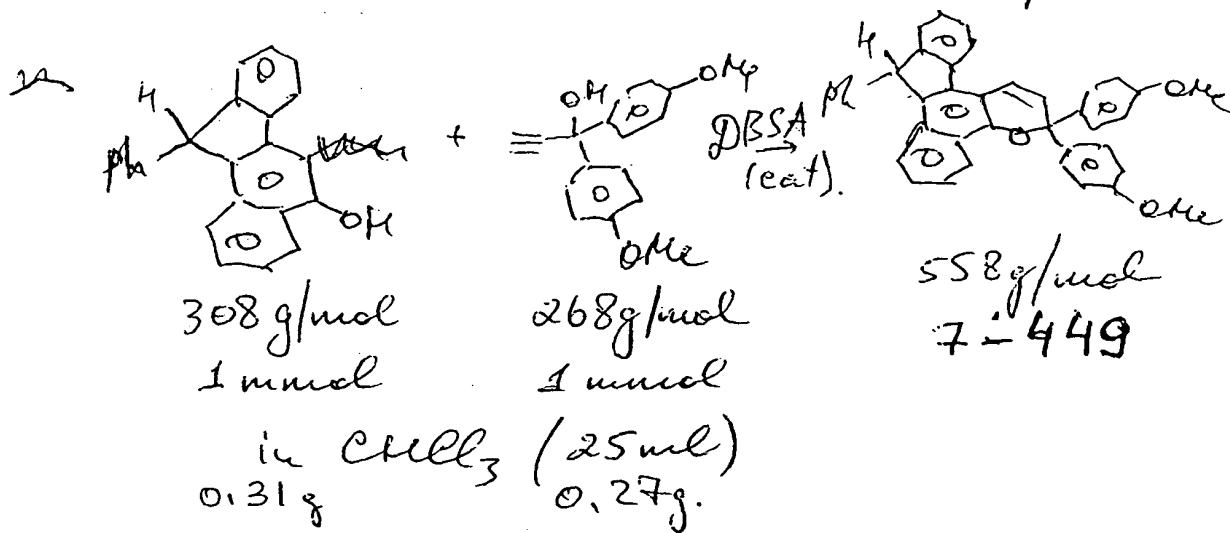
817-132a.



m.d.l

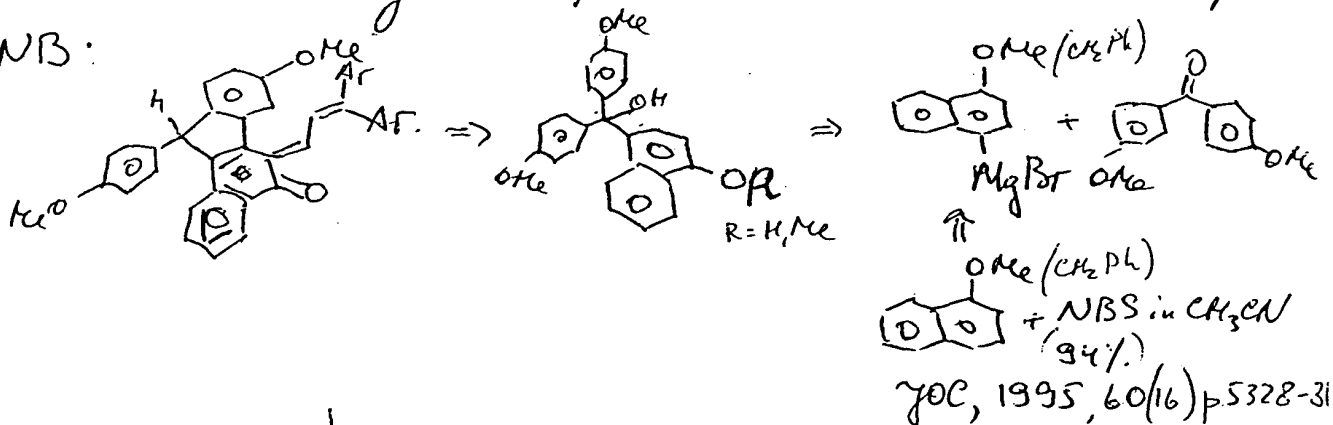
~~7-426~~
7-448

O.P.



stirred for 2 days at RT. Column: $\text{CH}_2\text{Cl}_2/\text{hex}$ (1:2), top spot is a photochromic compound. Collected 0.25 g \rightarrow 45%. UV-Vis: a double hump.

NB:



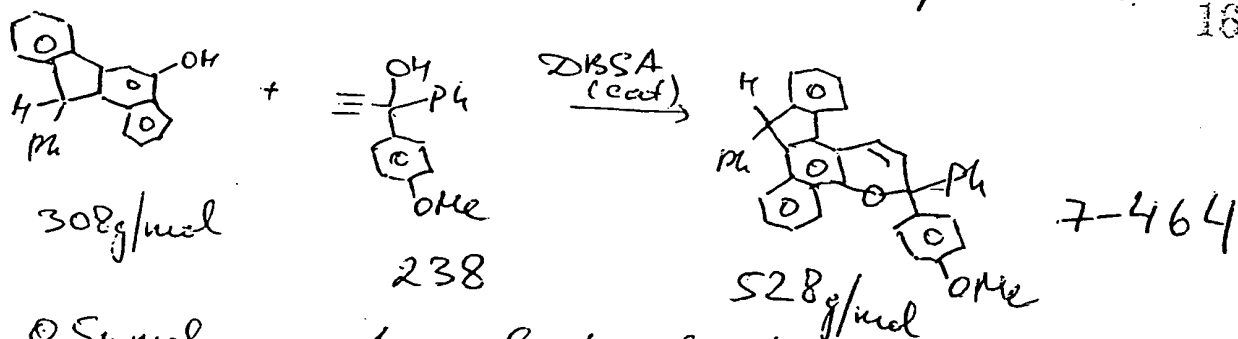
MS: 558 (good & pure)
 LC: 97.5%

m sl

O.P.

Shirley E. Williams

Witnessed page 147-158.



O. Samuel

1 mmol + 1 mmol a day later

200 ml CHCl_3 , 50 mg DBSulfonic acid.

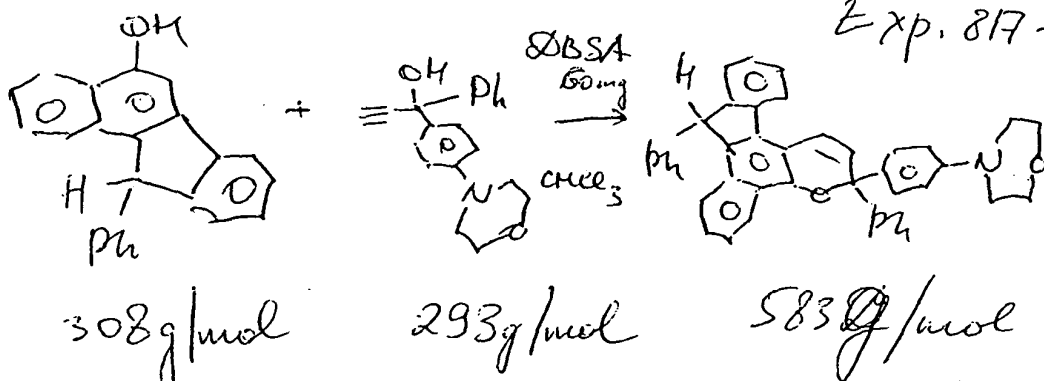
Stirred for one week. Column: CH_2Cl_2 /hexanes, 1/2. A red PC compound is isolated.

0.1 g, 0.19 mmol, 38% yield. HPLC: 2 peaks (diastereomeric), identical UV, 66% + 33% = 99% pure.

MS: 528 M^+ ; fragmentation is also consistent with the structure. 7.31.00: ^1H , ^{13}C confirm the structure.

O. P.

m. sl



1.23 g (4 mmol)

1.17 (4 mmol)

7-465

1) suspended in CHCl_3

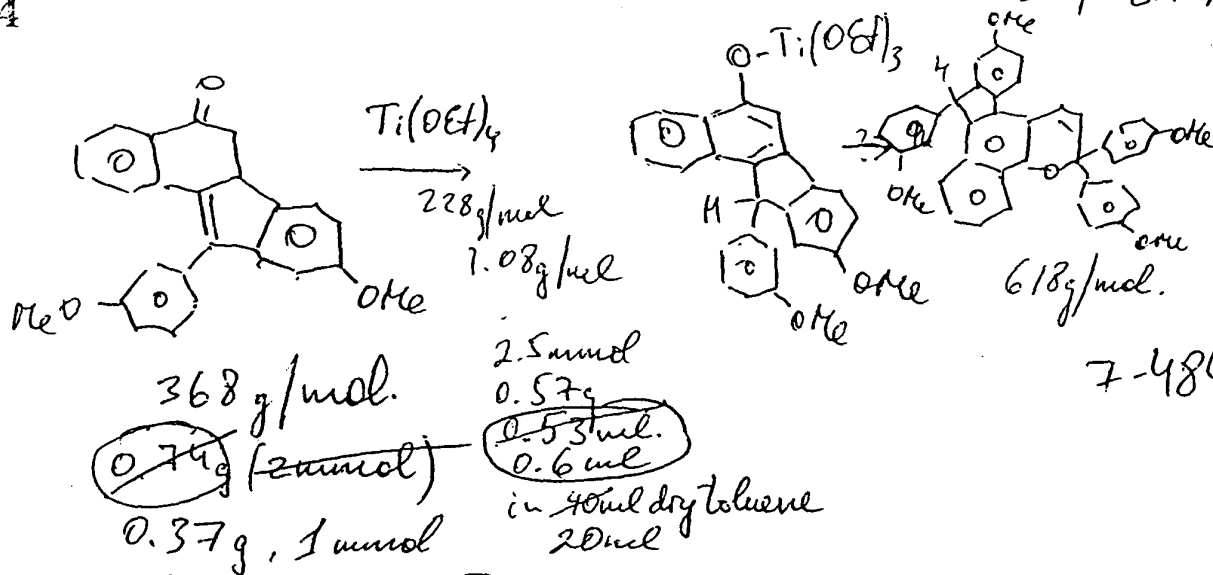
2) 60 mg DBSA added.

3) PA in 10 ml CHCl_3 added dropwise with stirring, over 2 hrs. Left to stir overnight.

Additional 110 mg of DBSA were added. The rxn. mix. was left to stir overnight. Stirring was continued for 2 days. Rxn. mixture was rotavaped and columned (CHCl_3 - bad idea.) The PC fractions (mixed) were collected and re-columned (10% EtOAc in hexanes). Triturated in EtCH_2CN (twice) (gray powder).
 MPLC purity: 98.5% (~1:1 mixture of diastereomers)
 $230 \text{ mg} + 110 \text{ mg} + 100 + 170 = 0.61 \text{ g} = 1.04 \text{ mmol}$, 26% of cryst. + filtrate.
 ^1H , ^{13}C NMR and MS confirm the structure.

m. d.

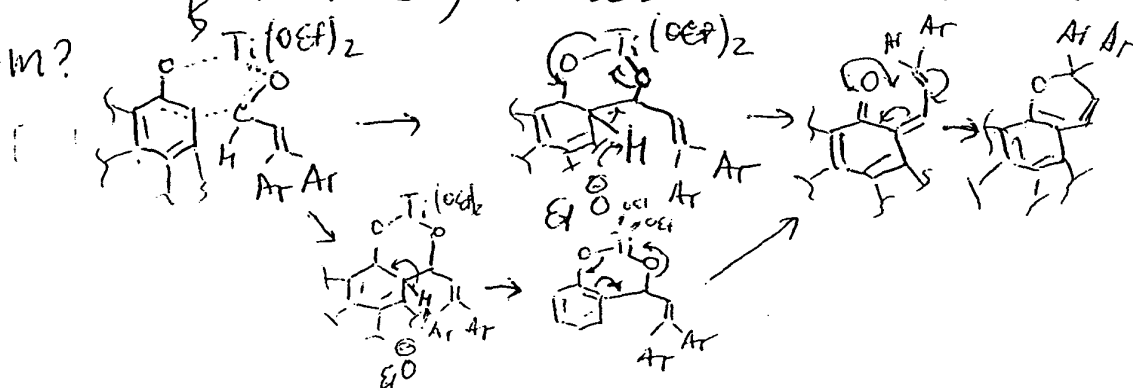
O. Petruskova



2 days at RT - no rxn.

Reflux in toluene for ~6 hrs, then 0.5 g of COc1ccc2c(c1)C(=O)C3=C(C=C2)C(=C(C=C3)OC)C4=CC=CC=C4 in 10 ml dry toluene were added. In 2 hrs TLC (EtOAc/CH₂Cl₂/hex, 1:4:5) shows PC formation.

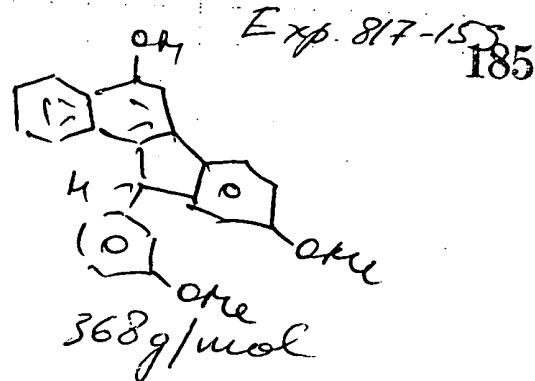
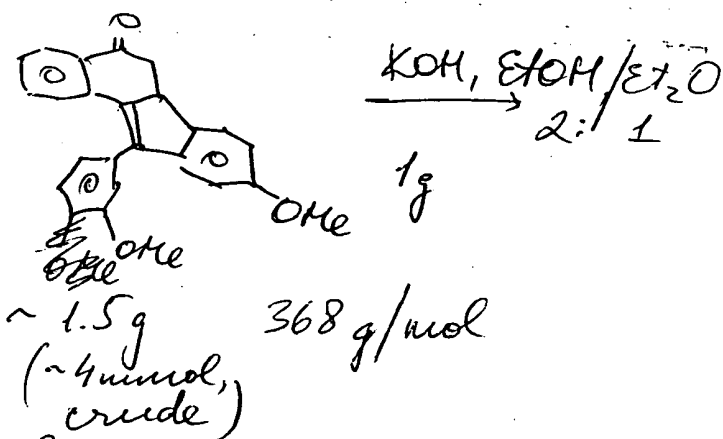
Mech-m?



Column: EtOAc/CH₂Cl₂/hex (1:4:5), then 1:4:15. Pure fraction: 0.2 g (> 97% pure by HPLC), 32% + mixed fractions (~0.1 mmol). Some st. m. (ketone) was recovered. MS OK.

Ma SL

O.P



From exp. 817-157

Workup: EtOH, Et₂O were removed (rotavap), MeCl (2M) was added to pH ~ 5. EtOAc extraction. $\Sigma \approx 1.9\text{g}$.

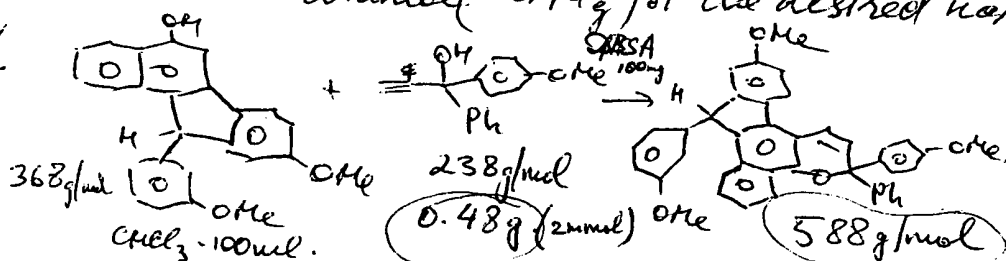
TLC (40% Et₂O/hex.): at least 2 spots. One is dark (reddish).



Does not react with PA₂

Exp. 817-160

assume ~2mmol (~0.74g) of the desired naphthol is present.



stirring, over night. TLC (4/MeOH/CH₂Cl₂): top spot is a PC, EtOAc/CH₂Cl₂/hex (1:4:5) works as well for separation. Another 0.24g of PA added, stirring was continued overnight.

Column: EtOAc/CH₂Cl₂/hex (1:4:5); top spot was isolated. Re-column 40% Et₂O/hex. The PC fractions were recryst. from MeOH - to no avail. Re-columned. Problem: large amt. of material separates in fractions of 55-85% purity. MS - OK.

me

O. P.